



AMENDMENTS TO THE CLAIMS

Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) A method for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a therapeutically effective amount of a recombinant polypeptide having the ability to bind TNF, wherein said polypeptide is encoded by a nucleic acid molecule comprising a the nucleotide sequence of the formula: $R^1-R^2-R^3-R^4$; wherein

R^1 is ATG, or the nucleotide sequence ATG-GGC-CTC-TCC-ACC-GTG-CCT-GAC-CTG-CTG-CTG-CCA-CTG-GTG-CTC-CTG-GAG-CTG-TTG-GTG-GGA-ATA-TAC-CCC-TCA-GGG-GTT-ATT-GGA (SEQ ID NO: 5), or is absent;

R^2 is the nucleotide sequence CTG-GTC-CCT-CAC-CTA-GGG-GAC-AGG-GAG-AAG-AGA (SEQ ID NO: 7) or is absent;

R^3 is the nucleotide sequence of SEQ ID NO: 3; and

R^4 is the nucleotide sequence GTT-AAG-GGC-ACT-GAG-GAC-TCA-GGC-ACC-ACA (SEQ ID NO: 9) or is absent as set forth in any of SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, residues 4 through 549 of SEQ ID NO: 9, residues 4 through 519 of SEQ ID NO: 15, or residues 4 through 516 of SEQ ID NO: 19.

2. (Amended) The method of Claim 1, wherein R^1 is ATG, R^2 is the nucleotide sequence CTG-GTC-CCT-CAC-CTA-GGG-GAC-AGG-GAG-AAG-AGA (SEQ ID NO: 7), and R^4 is the nucleotide sequence GTT-AAG-GGC-ACT-GAG-GAC-TCA-GGC-ACC-ACA (SEQ ID NO: 9) the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 9.

3. (Amended) The method of Claim 1, wherein R^1 is ATG, R^2 is the nucleotide sequence CTG-GTC-CCT-CAC-CTA-GGG-GAC-AGG-GAG-AAG-AGA (SEQ ID NO: 7), and R^4 is absent the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 15.

4. (Amended) The method of Claim 1, wherein R^1 is ATG, R^2 is absent, and R^4 is the nucleotide sequence GTT-AAG-GGC-ACT-GAG-GAC-TCA-GGC-ACC-ACA (SEQ ID NO: 9) the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 19.

5. (Amended) The method of Claim 1, wherein ~~R¹ is ATG, R² is absent, and R⁴ is absent~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 5.

6. (Amended) The method of Claim 1, wherein ~~R¹ is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R² is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R⁴ is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9)~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 7.

7. (Amended) The method of Claim 1, wherein ~~R¹ is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R² is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R⁴ is absent~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 13.

8. (Amended) The method of Claim 1, wherein ~~R¹ is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R² is absent, and R⁴ is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9)~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 11.

9. (Amended) The method of Claim 1, wherein ~~R¹ is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R² is absent, and R⁴ is absent~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 17.

10. (Amended) The method of Claim 1, wherein ~~R¹ is absent, R² is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R⁴ is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9)~~

the nucleic acid molecule comprises residues 4 through 549 of the nucleotide sequence as set forth in SEQ ID NO: 9.

11. (Amended) The method of Claim 1, wherein ~~R¹ is absent, R² is the nucleotide sequence CTG-GTC-CCT-CAC-CTA-GGG-GAC-AGG-GAG-AAG-AGA (SEQ ID NO: 7), and R⁴ is absent~~ the nucleic acid molecule comprises residues 4 through 519 of the nucleotide sequence as set forth in SEQ ID NO: 15.

12. (Amended) The method of Claim 1, wherein ~~R¹ is absent, R² is absent, and R⁴ is the nucleotide sequence GTT-AAG-GGC-ACT-GAG-GAC-TCA-GGC-ACC-ACA (SEQ ID NO: 9)~~ the nucleic acid molecule comprises residues 4 through 516 of the nucleotide sequence as set forth in SEQ ID NO: 19.

13. (Amended) The method of Claim 1, wherein ~~R¹ is absent, R² is absent, and R⁴ is absent~~ the nucleic acid molecule comprises the nucleotide sequence as set forth in SEQ ID NO: 3.

15. (Amended) A method for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a therapeutically effective amount of a recombinant polypeptide having the ability to bind TNF, wherein said polypeptide comprises ~~an~~ the amino acid sequence of the formula: R¹-R²-R³-R⁴, wherein

~~R¹ is methionine, or the amino acid sequence Met-Gly-Leu-Ser-Thr-Val-Pro-Asp-Leu-Leu-Leu-Pro-Leu-Val-Leu-Leu-Glu-Leu-Leu-Val-Gly-Ile-Tyr-Pro-Ser-Gly-Val-Ile-Gly (SEQ ID NO: 6), or is absent;~~

~~R² is the amino acid sequence Leu-Val-Pro-His-Leu-Gly-Asp-Arg-Glu-Lys-Arg (SEQ ID NO: 8) or is absent;~~

~~R³ is the amino acid sequence of SEQ ID NO: 4; and~~

~~R⁴ is the amino acid sequence Val-Lys-Gly-Thr-Glu-Asp-Ser-Gly-Thr-Thr (SEQ ID NO: 10) or is absent~~ as set forth in any of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, residues 2 through 183 of SEQ ID NO: 10, residues 2 through 173 of SEQ ID NO: 16, or residues 2 through 172 of SEQ ID NO: 20; and

wherein said polypeptide has:

- a) at least one conservative amino acid substitution;
- b) at least one amino acid substitution at a glycosylation site;
- c) at least one amino acid substitution at a proteolytic cleavage site;
- d) at least one amino acid substitution at a cysteine residue;
- e) at least one amino acid deletion;
- f) at least one amino acid insertion;
- g) a C- and/or N-terminal truncation; or
- h) a combination of modifications selected from the group consisting of conservative

amino acid substitutions, amino acid substitutions at a glycosylation site, amino acid substitutions at a proteolytic cleavage site, amino acid substitutions at a cysteine residue, amino acid deletions, amino acid insertions, C-terminal truncation, and N-terminal truncation.

16. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises~~ an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and has at least one conservative amino acid substitution.

17. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises~~ an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and has at least one amino acid substitution at a glycosylation site.

18. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises~~ an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and has at least one amino acid substitution at a proteolytic cleavage site.

19. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises~~ an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and has at least one amino acid substitution at a cysteine residue.

20. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises~~ an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and has at least one amino acid deletion.

21. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and~~ has at least one amino acid insertion.

22. (Amended) The method of Claim 15, wherein said encoded polypeptide ~~comprises an amino acid sequence of the formula: $R^1-R^2-R^3-R^4$ and~~ has a C- and/or N-terminal truncation.

23. (Amended) A method for ameliorating the harmful effects of TNF in an animal, comprising administering to an animal in need of such treatment a therapeutically effective amount of a recombinant polypeptide having the ability to bind TNF, wherein said polypeptide comprises ~~an~~ the amino acid sequence ~~of the formula: $R^1-R^2-R^3-R^4$, wherein~~

~~R^1 is methionine, or the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), or is absent;~~

~~R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8) or is absent;~~

~~R^3 is the amino acid sequence of SEQ ID NO: 4; and~~

~~R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10) or is absent as set forth in any of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, residues 2 through 183 of SEQ ID NO: 10, residues 2 through 173 of SEQ ID NO: 16, or residues 2 through 172 of SEQ ID NO: 20.~~

24. (Amended) The method of Claim 23, wherein ~~R^1 is methionine, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 10.

25. (Amended) The method of Claim 23, wherein ~~R^1 is methionine, R^2 is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R^4 is absent~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 16.

26. (Amended) The method of Claim 23, wherein ~~R¹ is methionine, R² is absent, and R⁴ is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 20.

27. (Amended) The method of Claim 23, wherein ~~R¹ is methionine, R² is absent, and R⁴ is absent~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 6.

28. (Amended) The method of Claim 23, wherein ~~R¹ is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R² is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R⁴ is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 8.

29. (Amended) The method of Claim 23, wherein ~~R¹ is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R² is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R⁴ is absent~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 14.

30. (Amended) The method of Claim 23, wherein ~~R¹ is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R² is absent, and R⁴ is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 12.

31. (Amended) The method of Claim 23, wherein ~~R¹ is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R² is absent, and R⁴ is absent~~ said encoded polypeptide

comprises the amino acid sequence as set forth in SEQ ID NO: 18.

32. (Amended) The method of Claim 23, wherein ~~R¹ is absent~~, ~~R² is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8)~~, and ~~R⁴ is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~, said encoded polypeptide comprises residues 2 through 183 of the amino acid sequence as set forth in SEQ ID NO: 10.

33. (Amended) The method of Claim 23, wherein ~~R¹ is absent~~, ~~R² is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8)~~, and ~~R⁴ is absent~~ said encoded polypeptide comprises residues 2 through 173 of the amino acid sequence as set forth in SEQ ID NO: 16.

34. (Amended) The method of Claim 23, wherein ~~R¹ is absent~~, ~~R² is absent~~, and ~~R⁴ is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10)~~ said encoded polypeptide comprises residues 2 through 172 of the amino acid sequence as set forth in SEQ ID NO: 20.

35. (Amended) The method of Claim 23, wherein ~~R¹ is absent~~, ~~R² is absent~~, and ~~R⁴ is absent~~ said encoded polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 4.